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Early Carotid Endarterectomy after Non-disabling Ischaemic Stroke: Adequate Therapeutical Option in Selected Patients*

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Objective: *To evaluate neurological outcome and long-term results of early carotid endarterectomy (CEA) after non-disabling stroke.*
Materials: *Retrospective study between 1980 and 1995 of 56 patients undergoing CEA within 4 weeks of a transient (n=15) or a permanent non-disabling (n=41) ischaemic stroke.*
Methods: *Analyses of preoperative cerebral CT imaging, neurological outcome (mod. Rankin-scale) and long-term results (life-table analyses according to Kaplan–Meier).*
Results: *Incidence of early CEA increased from 1.7% (27 out of 1636) in the period 1980–1993 to 7.8% (29 out of 374) between 1994 and 1995. CEA was indicated after a neurological plateau phase was established (median interval 14 days). Fifty-seven per cent of the CEA patients had a minor ischaemic infarction (area <2 cm), 18% showed a large territorial ischaemic infarction (area 2–5 cm) in cerebral CT imaging. Two patients deteriorated postoperatively (minor stroke rate 4%) but no major stroke or death occurred. Life-table probability of stroke-free survival (mean follow-up 42.7 months) was 94%, 90% and 84%, respectively, after 1, 2 and 5 years. Kaplan-Meier survival rates were 96%, 91% and 86% after 1, 2 and 5 years.*
Conclusions: *Early CEA after non-disabling stroke is a safe procedure in selected patients.*

Key Words: Carotid endarterectomy; Early period; Non-disabling stroke; Neurological outcome.

Introduction

The effectiveness of elective carotid endarterectomy (CEA) in the secondary prevention of ischaemic stroke due to high-grade symptomatic carotid bifurcation atherosclerosis is well established and generally accepted since the results of both multicentre trials ECST and NASCET were published.[1,2] In contrast, the indications for carotid disobliteration in the early period after transient or non-disabling stroke remain controversial. Traditionally, a delay of at least 6 weeks is recommended for CEA in those patients who are considered to be both neurologically unstable and at high risk of secondary intracerebral bleeding into the ischaemic infarction area.[3,4] However, patients with symptomatic extracranial carotid disease are exposed to a significant risk of recurrent stroke (5%–9.5%) within 30 days after the initial event. This strongly supports the therapeutic option of early eradication of the embolic carotid source following neurological improvement.[5–8]

Between 1980 and 1993, 27 CEA out of a total of 1,636 CEAs (1.7%) being performed in our Department were classified as "early", i.e. within 4 weeks after an initial transient or permanent minor stroke. This quantity has steadily increased up to 7.6% in the period 1994–1995 ($n=29$ out of 377). The aim of this study was to analyse those patients with regard to indication, neurological outcome and long-term results. The main question is whether an increasing proportion of early CEAs in the first weeks after a carotid-related stroke might be justified by clinical results.

Patients and Methods

Two thousand and thirteen carotid reconstructions were performed in our Department between January 1980 and December 1995: 1909 CEAs (94.8%) were

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performed electively (mortality rate 0.6%, major stroke rate 1.3%, combined minor and major stroke rate 2.3%) and 48 patients (2.4%) were operated on an emergency basis (acute/progressive stroke, crescendo TIAs).

The study population consisted of 56 CEAs (2.8%) performed within 4 weeks (median 14 days, range 5–27 days) after a temporary stroke (neurological deficit >24 h but complete recovery preoperatively) or a permanent non-disabling ischaemic stroke in the carotid territory. All patients were transferred from the Department of Neurology, and were clinically assessed according to the modified Rankin-scale in the pre- and postoperative period. Selection criteria for early CEA included: (1) suitable carotid lesions; (2) focal neurological deficit in the distribution of the carotid territory which was non-disabling, or (3) had remarkably improved within a few days (neurological plateau phase). Contraindications for CEA in the early period after an ischaemic stroke were as follows: (1) impaired consciousness and/or haemorrhagic infarction on CT scan, (2) patients with organ failure or myocardial infarction and (3) patients who were confined to bed or wheelchairs.

Patient data were retrospectively analysed before 1993 and prospectively since 1994. Patient characteristics included age, sex, risk profile and results of both cerebral CT imaging and carotid angiography. Preoperative CT scans of the brain were grouped as following: no evidence of ischaemic lesion; minor ischaemic infarction (area <2 cm); large territorial ischaemic infarction (area >2 cm) in the anterior circulation. Carotid lesions were assessed angiographically as high-grade carotid stenosis (70% or more), pseudo-occlusions (subtotal stenosis with delayed, but orthograde fillings of the internal carotid artery, angiographically described as "string sign"), deep ulceration in the absence of a high-grade stenosis and carotid aneurysm respectively. Follow-up was predominantly obtained by outpatient re-evaluation. Telephone interviews with general physicians or with relatives were only used in cases of disability or death. Outcome events were: (1) ipsilateral stroke classified as major (disabling) or minor (non-disabling); (2) combined ipsi- and contralateral stroke and (3) death rate. Life-table analysis was by the Kaplan–Meier method.

Results

Patient characteristics

The mean age of our 56 patients was 62 years (range 41–86 years) without any significant difference between the two major groups. Twenty-five per cent were women ($n=14$) and 75% men. Mean follow-up was 42.7 months (range 2–178 months). One patient had a symptomatic recurrent carotid artery stenosis and four patients had undergone contralateral CEA 1–165 months before. Hypertension was the most common risk factor in these 56 patients (64%). Forty-seven per cent were smokers, followed by disorders of lipid metabolism in 39.5%, chronic obstructive or restrictive pulmonary insufficiency in 23.5%, diabetes mellitus in 22% and renal insufficiency (serum creatinine >1.3 mg%) in 7%. Forty-nine per cent of patients had a history of coronary artery disease with evidence of myocardial infarction or angina pectoris.

Fifteen patients were operated on after a transient stroke and 41 patients after a permanent minor stroke within 5–27 days (median 14 days). According to the modified Rankin-scale, 37.5% of the patients had no or only a minimal preoperative deficit (Rankin 0/1), 55% had a mild or moderate neurological deficit and were able to walk (Rankin 2/3), while 7% had remarkably improved but were not yet able to walk alone without some support (Rankin 4). There was no evidence of ischaemic lesions on CT scanning in 25%, a minor ischaemic infarction (ø<2 cm) in 57.1% and a large territorial ischaemic infarction (ø>2 cm, in the distribution area of the middle and/or anterior cerebral artery) in 17.9% (Table 1). In eight patients with large cerebral infarction the postoperative cerebral CT scan did not show any deterioration or signs of intracerebral bleeding.

Operative details

Since 1992, surgery was performed in 36 of these patients using *somatory-sensory evoked potentials (SSEP)* monitoring. Loss of SSEP and/or the existence of a minimal, non-pulsatile stump pressure required the insertion of an indwelling ,shunt. In 12 of these 36 patients (33%) neuro-monitoring by SSEPs were not reliable due to insufficient basic measurements.

Early CEA was performed for high-grade ICA stenosis (>70%) in 48 out of 56 patients. Four carotid aneurysms and/or moderate ulcerated carotid stenoses were treated by CEA or vein-graft interposition. In one patient preoperative thrombolysis of an acute ICA occlusion was successful and revealed a carotid pseudo-occlusion. After 6 days this pseudo-occlusion was found to be definitely reoccluded at operation. Fortunately the patient did not suffer a worsening of his pre-existing neurological deficit. In another three patients a carotid pseudo-occlusion was successfully recanalised by CEA (Table 1).

Table 1. Early CEA (ø 14 days) after a transient/non-disabling stroke: preoperative CT scan of the brain, intraoperative findings and neurological outcome.

		Transient stroke ($n=15$)	Permanent stroke ($n=41$)	Transient/permanent stroke ($n=56$)
Preoperative CT scan				
	No ischaemic lesion	60%	12.2%	25%
	Cerebral infarction <2 cm ø	26.7%	68.3%	57.1%
	Cerebral infarction >2 cm ø	13.3%	19.5%	17.9%
Somato-sensory-evoked potentials ($n=36$)				
	Good, judgeable	80%	64.5%	66.7%
	Moderate/not judgeable	20%	35.5%	33.3%
Lesions of the ICA				
	Occlusions	—	1 (No deficit)	1 (No deficit)
	Pseudo-occlusion	1	2	3
	High-grade stenosis	13	3	48
	Aneurysm/ulcer	1	3	4
Neurological outcome				
	No new symptoms	100%	95.1%	96.4%
	Minor worsening (no intracerebral bleeding)	—	4.9%	3.6%
	Major stroke/mortality	—	—	—

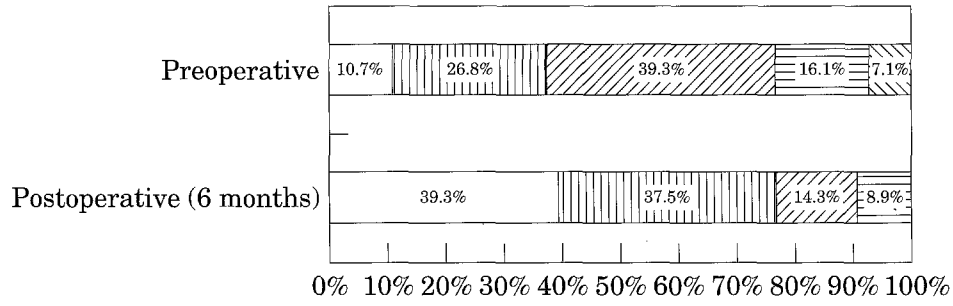

Fig.1. Pre- and postoperative neurological assessment in early CEA (ø 14 days) after a transient/non-disabling stroke ($n=56$, modified Rankin-scale). (□) Recovery (Rankin 0); (▨) mild deficit, independent (Rankin 2); (▧) severe deficit, not walking alone (Rankin 4); (■) perioperative death (Rankin 6); (▥) minimal deficit (Ranking 1); (□) moderate deficit, little support (Rankin 3), (▦) confined to bed/wheelchair (Rankin 5).

Neurological outcome

No patient died perioperatively and no major stroke occurred. Two out of 56 patients suffered a minor worsening of their preoperative paresis, resulting in a minor stroke rate of 4%. The cerebral CT scans did not show any deterioration of the pre-existing ischaemic infarction. After 6 months 79% of patients had totally recovered or were suffering only minimal deficit (Rankin 0/1). Twenty-three per cent had a mild or moderate deficit but no patient was classified as Rankin 4. Figure 1 illustrates the preoperative neurological scoring and the eventual outcome after 6 months.

Long-term results (Figs 2, 3 and 4)

During follow-up, eight patients died after a mean interval of 40 months (range 13–83 months) by myocardial infarction ($n=3$), malignancy ($n=2$), suicide ($n=1$) or unknown cause ($n=2$). Using Kaplan–Meier life-table analysis, survival rates after 1, 2 and 5 years are 96%, 91% and 86% (mean follow-up interval 42.7 months, range 2–178 months). No ipsilateral major or fatal stroke occurred during follow-up. The life-table probability of any major or minor ipsilateral stroke was 94.5% for all three intervals and 94%, 90% and 83% for any ipsi- or contralateral stroke after 1, 2 and 5 years, respectively.

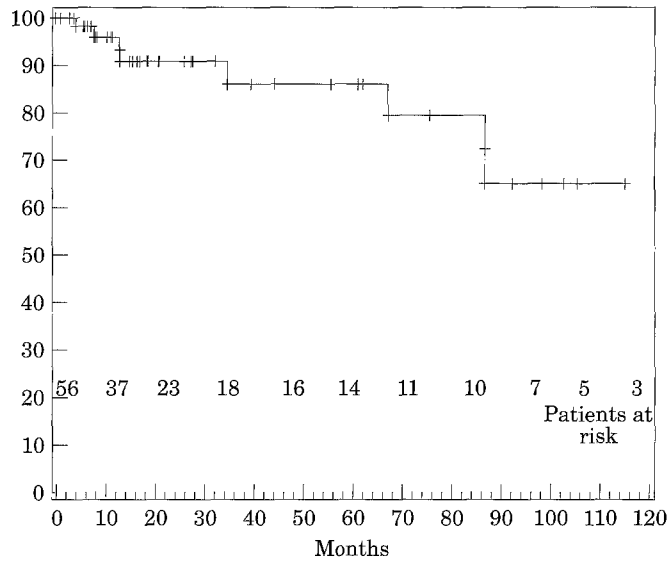

Fig. 2. Long-term survival after early CEA in 56 patients with a transient or non-disabling carotid stroke (Kaplan–Meier).

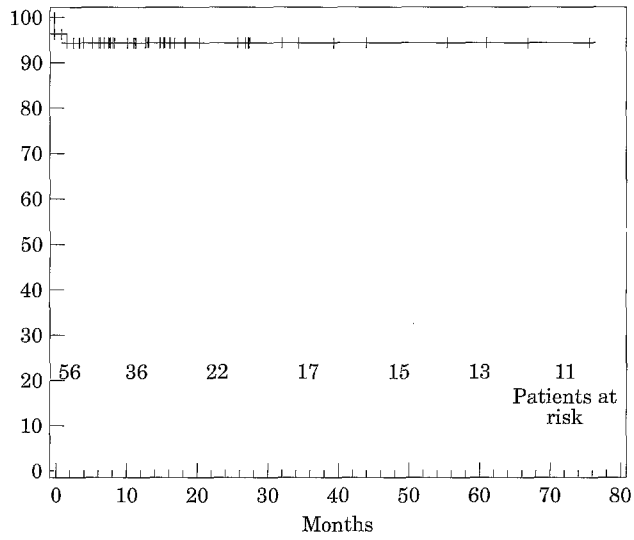

Fig. 3. Probability of any ipsilateral stroke-free survival after early CEA in 56 patients with a transient or a non-disabling carotid stroke (Kaplan–Meier, including perioperative strokes).

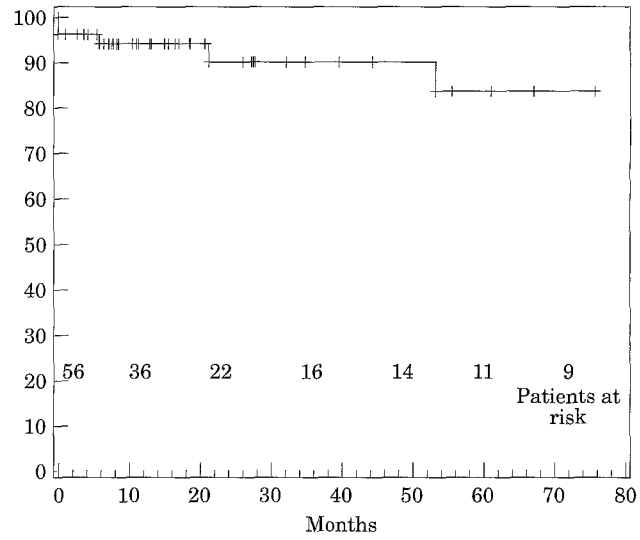

Fig. 4. Probability of any ipsi- or contralateral stroke-free survival after early CEA in 56 patients with a transient or a non-disabling carotid stroke (Kaplan–Meier, including perioperative strokes).

Discussion

Eradication of the embolic source and restoration of cerebral blood flow to reperfuse ischaemic but non-infarcted areas of the brain (ischaemic penumbra) are the rationales for early endarterectomy in carotid-related ischaemic strokes.

Based on poor results in early studies, patients in the early phase after an ischaemic stroke traditionally are considered to be neurologically unstable.[3,4,9,10] The Joint Study of Extracranial Artery Occlusion resulted in a mortality and stroke rate of 42% compared to 20% in the conservative treatment group, which suggested that CEA within 2 weeks after an acute stroke carried a high risk of converting a bland infarct to a haemorrhagic one.[3] In retrospect it is possible that inadequate patient selection with poor preoperative identification of the degree of the cerebral injury in the era before CT and MRI, and insufficient control of postoperative hypertension, might have contributed to the high incidence of perioperative cerebral haemorrhage.

Prospective studies show that even the early period after the initial stroke has a high risk for stroke recurrence. Hier *et al.* found a 2-year cumulative recurrence rate of 14%. Thirty per cent of these recurrences occurred within 30 days, especially in

atherosclerotic strokes.[11] In the Oxfordshire Community Stroke Project the prevalence of a 70–99% stenosis or occlusion of the internal carotid artery in patients with a partial or a total anterior cerebral infarction was about 30%.[12] Follow-up in patients with partial anterior cerebral infarction revealed a recurrence rate of 17% within 1 year, with a maximum in the first few months, supporting the hypothesis of an active embolising carotid lesion. This presumption is supported by the fact that in the NASCET study 4.9% of 103 medically treated patients diagnosed with symptoms of a minor carotid-related stroke had a recurrent ipsilateral stroke within 30 days.[7] In retrospective series a recurrence rate of 9.5% at 6 weeks after an initial stroke has been reported.[6]

Due to a lack of randomised trials the risk/benefit ratio of conservative or early CEA is controversial.[13–16] The analysis of 42 out of 100 NASCET-patients operated on within 4 weeks after a non-disabling stroke (median 16 days, 3–30 days) revealed a perioperative ischaemic stroke rate of 4.8%, while 58 patients who had surgery after 30 days resulted in a perioperative stroke rate of 5.2%. In the early group both strokes were major in severity, as the result of acute occlusion at the endarterectomy site 2 and 3 hours postoperatively, representing technical failures of the procedure unrelated to the timing of surgery. Both patients had normal preoperative CT scanning.[7] Piotrowski *et al.* studied 82 patients with an acute stroke in whom CEA was performed after reaching a neurological plateau within 1–6 weeks.[14] No significant difference in morbidity/mortality was found between patients operated on at 2, 4 or 6 weeks after stroke and between patients who were operated on after a delay of 6 weeks (2.4% vs. 6.3%). In their entire group only one haemorrhagic stroke occurred postoperatively, probably due to poorly controlled perioperative hypertension. In another series, 28 patients with a small fixed neurological deficit, early CEA was performed after a mean interval of 11 days after stroke. Operative mortality consisted of one death from a pulmonary embolus and no patient sustained a new postoperative neurological deficit.[15] These results are in disagreement with only one modern series presented by Giordano *et al.*, who considered early CEA to be contraindicated in the early period after stroke as 5 out of 24 patients operated on within 5 weeks suffered a perioperative stroke but 0 out of 22 operated on beyond 5 weeks did not (Table 3).[13]

The majority of reports indicate that the risk of surgery within 4 weeks after a carotid-related non-disabling stroke does not exceed 5%.[17–19] In our series the minor ischaemic stroke rate postoperatively was 4% in 56 patients with a minor or transient stroke and 5% in patients with minor strokes alone (2 out of 41 patients). In both stroke patients no intracerebral haemorrhage was detectable on CT scan postoperatively, confirming the view that the blood–brain barrier seems to be rapidly repaired after an ischaemic stroke. Similarly, the NASCET collaborators did not find any case of postoperative intracerebral haemorrhage after early surgery, as the one instance in their series occurred 6 days postoperatively in a patient with an abnormal CT scan who underwent operation 54 days after the presenting stroke.[7] As indicated by larger series, development of intracerebral haemorrhage following CEA may not necessarily be related to the timing of operation and to the size of the preoperative infarction. In Pomposelli's series, cerebral haemorrhage occurred in 11 of 1500 patients in the immediate postoperative period after CEA. No patient had suffered a recent stroke. Moreover, all of the cerebral haemorrhage patients had carotid stenosis greater than 90%.[20] Loss of cerebral autoregulation, hypertension and marked increase in blood flow may increase the risk of cerebral bleeding in patients with severe carotid stenosis, confirming the view that control of perioperative hypertension is essential.

Intraoperative neuro-monitoring by SSEP is not as useful in early CEA compared to elective CEA.[21] In our experience 33% of patients could not be monitored by SSEP, probably due to the cerebral infarction in the distribution of the middle cerebral artery. This led to a higher frequency of CEAs performed with shunt protection. The long-term results after early CEA following a non-disabling stroke are also promising and comparable to those after elective CEA in symptomatic carotid disease: Piotrowski *et al.* reported a survival rate of 84% and an absence of any further stroke of 91% after 5 years.[14] Similarly the survival rate of our patient group was 86% after 5 years and 94% and 83% of our patients were free of any further ipsi- or contralateral stroke, respectively, within 5 years after CEA. It is of note that Dr DeBakey's first CEA in the world in August 1953 was performed 8 days after a minor stroke. The outcome for this patient was excellent: he totally recovered and survived for 22 years.[22]

In summary, this study indicates that early CEA after a non-disabling carotid-related stroke can be safely performed in properly-selected patients (appropriate carotid lesion, carotid-related ischaemic stroke, no haemorrhage on cerebral CT, no alteration of consciousness). In order to determine the risks and benefits of early CEA we have now initiated a multicentre observation study called Carotid Surgery for Ischaemic Stroke (CASIS). In order to obtain data

Table 2. Early CEA after a transient or non-disabling stroke: stroke and mortality rates in the literature.

Author	Patients	CT scan of the brain	Interval	Stroke rate	Mortality
Whittemore 1984	$n=28$	65% ipsilateral infarct	ø 11 days	—	1 (3.6%)
Dosick 1985	$n=110$	Yes: no infarct	<2 weeks (ø 10 days)	$n=1$ (0.9%)	—
Giordano 1985	$n=24$	Yes	<5 weeks (ø 18 days)	$n=5$ (18.5%)	—
Piotrowski 1990	$n=82$	71% ipsilateral infarct	<6 weeks	$n=1$ (1.2%)	1 (1.2%)
Gasecki (NASCET) 1994	$n=42$	40% ipsilateral infarct	Median 16 days (3–30 days)	$n=2$ (4.8%)*	—
Eckstein/Heidelberg 1998	$n=56$	75% ipsilateral infarct	Median 14 days (5–27 days)	$n=2$ (3.6%)†	–

* Major ischaemic ipsilateral strokes due to acute carotid occlusion 2 and 3 h postoperatively (technical failure);
† minor ipsilateral strokes, no new ischaemic/haemorrhagic infarction on CT (<ø 2 cm ischaemic stroke preoperatively).

about the overall incidence of carotid-related strokes, participating centres register all carotid-related strokes and select those patients with a transient or a non-disabling stroke who may be good candidates for carotid surgery. The interval between the onset of stroke and CEA is not determined by study protocol but can be individually judged. In order to get a sufficient number of participating centres, the interval for "early" surgery has been extended to 6 weeks. The main end-points for CASIS are as following: (1) incidence of recurrent stroke between first onset of stroke and carotid surgery, (2) incidence of intracerebral haemorrhage postoperatively, confirmed by CT scan of the brain and (3) neurological outcome, assessed by use of neurological scores (modified Rankin-scale, European Stroke Scale) pre- and postoperatively. CASIS is open to any centre in whom a co-operation between Departments of Neurology and Vascular Surgery has been established and carotid surgery within 6 weeks after a non-disabling ischaemic strokes can be performed. Analysis of data will be on an intention-to-treat basis.

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